

1/40

SEQUENCE LISTING

<110> TRANSGENE S.A.

<120> Novel multifunctional cytokines

<130> TG163

<160> 59

<170> PatentIn version 3.1

<210> 1

<211> 345

<212> PRT

<213> artificial sequence (fusion human IL-7/linker/human IL-2)

<400> 1

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Leu Pro Pro Leu Ile
1 5 10 15

Leu Val Leu Leu Pro Val Ala Ser Ser Asp Cys Asp Ile Glu Gly Lys
20 25 30

Asp Gly Lys Gln Tyr Glu Ser Val Leu Met Val Ser Ile Asp Gln Leu
35 40 45

Leu Asp Ser Met Lys Glu Ile Gly Ser Asn Cys Leu Asn Asn Glu Phe
50 55 60

Asn Phe Phe Lys Arg His Ile Cys Asp Ala Asn Lys Glu Gly Met Phe
65 70 75 80

Leu Phe Arg Ala Ala Arg Lys Leu Arg Gln Phe Leu Lys Met Asn Ser
85 90 95

Thr Gly Asp Phe Asp Leu His Leu Leu Lys Val Ser Glu Gly Thr Thr
100 105 110

Ile Leu Leu Asn Cys Thr Gly Gln Val Lys Gly Arg Lys Pro Ala Ala
115 120 125

Leu Gly Glu Ala Gln Pro Thr Lys Ser Leu Glu Glu Asn Lys Ser Leu
130 135 140

Lys Glu Gln Lys Lys Leu Asn Asp Leu Cys Phe Leu Lys Arg Leu Leu
145 150 155 160

Gln Glu Ile Lys Thr Cys Trp Asn Lys Ile Leu Met Gly Thr Lys Glu
165 170 175

His Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
180 185 190

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
195 200 205

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
210 215 220

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
225 230 235 240

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
245 250 255

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
260 265 270

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
275 280 285

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
290 295 300

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
305 310 315 320

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
325 330 335

Cys Gln Ser Ile Ile Ser Thr Leu Thr
340 345

<211> 333

<212> PRT

<213> artificial sequence (fusion murine IL7/linker/murine IL-2)

<400> 2

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Ile Pro Pro Leu Ile
 1 5 10 15

Leu Val Leu Leu Pro Val Thr Ser Ser Glu Cys His Ile Lys Asp Lys
 20 25 30

Glu Gly Lys Ala Tyr Glu Ser Val Leu Met Ile Ser Ile Asp Glu Leu
 35 40 45

Asp Lys Met Thr Gly Thr Asp Ser Asn Cys Pro Asn Asn Glu Pro Asn
 50 55 60

Phe Phe Arg Lys His Val Cys Asp Asp Thr Lys Glu Ala Ala Phe Leu
 65 70 75 80

Asn Arg Ala Ala Arg Lys Leu Lys Gln Phe Leu Lys Met Asn Ile Ser
 85 90 95

Glu Glu Phe Asn Val His Leu Leu Thr Val Ser Gln Gly Thr Gln Thr
 100 105 110

Leu Val Asn Cys Thr Ser Lys Glu Glu Lys Asn Val Lys Glu Gln Lys
 115 120 125

Lys Asn Asp Ala Cys Phe Leu Lys Arg Leu Leu Arg Glu Ile Lys Thr
 130 135 140

Cys Trp Asn Lys Ile Leu Lys Gly Ser Ile Gly Gly Gly Gly Ser Gly
 145 150 155 160

Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu
 165 170 175

Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser
 180 185 190

Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln
 195 200 205

Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser
 210 215 220

Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe
225 230 235 240

Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys
245 250 255

Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln
260 265 270

Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile
275 280 285

Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys
290 295 300

Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp
305 310 315 320

Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln
325 330

<210> 3

<211> 330

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/human IL-15)

<400> 3

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly
 145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Met Arg Ile Ser Lys Pro His Leu
 165 170 175

Arg Ser Ile Ser Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His
 180 185 190

Phe Leu Thr Glu Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser
 195 200 205

Ala Gly Leu Pro Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp
 210 215 220

Leu Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr
 225 230 235 240

Leu Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met
 245 250 255

Lys Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp
 260 265 270

Ala Ser Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn
 275 280 285

Ser Leu Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys
 290 295 300

Glu Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val
 305 310 315 320

His Ile Val Gln Met Phe Ile Asn Thr Ser
 325 330

<211> 330

<212> PRT

<213> artificial sequence (fusion human IL-15/linker/human IL-2)

<400> 4

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
 1 5 10 15

Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His
 20 25 30

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
 35 40 45

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
 50 55 60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
 65 70 75 80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
 85 90 95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
 100 105 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
 115 120 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
 130 135 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
 145 150 155 160

Thr Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
 165 170 175

Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala
 180 185 190

Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln
 195 200 205

Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly

210

215

220

Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys
 225 230 235 240

Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu
 245 250 255

Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser
 260 265 270

Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val
 275 280 285

Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr
 290 295 300

Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr
 305 310 315 320

Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
 325 330

<210> 5

<211> 350

<212> PRT

<213> artificial sequence (fusion signal IL-2/ human IL-15/linker/human
 IL-2)

<400> 5

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15

Val Thr Asn Ser Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser
 20 25 30

Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu
 35 40 45

Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro
 50 55 60

Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile
 65 70 75 80

Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu
85 90 95

Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu
100 105 110

Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His
115 120 125

Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser
130 135 140

Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu
145 150 155 160

Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln
165 170 175

Met Phe Ile Asn Thr Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
180 185 190

Gly Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala
195 200 205

Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr
210 215 220

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
225 230 235 240

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
245 250 255

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
260 265 270

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
275 280 285

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
290 295 300

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
305 310 315 320

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
325 330 335

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Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
340 345 350

<210> 6

<211> 324

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine IL-15)

<400> 6

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr
180 185 190

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Leu Val Leu Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg
195 200 205

Tyr Asp Leu Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp
210 215 220

Thr Thr Leu Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr
225 230 235 240

Ala Met Asn Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr
245 250 255

Ser Asn Met Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala
260 265 270

Asn Ser Thr Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys
275 280 285

Glu Cys Glu Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser
290 295 300

Phe Ile Arg Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp
305 310 315 320

Asp Asp Asp Lys

<210> 7

<211> 324

<212> PRT

<213> artificial sequence (fusion murine IL-15/linker/murine IL-2)

<400> 7

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg Tyr Asp Leu
20 25 30

Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp Thr Thr Leu
35 40 45

Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr Ala Met Asn
50 55 60

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Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr Ser Asn Met
65 70 75 80

Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala Asn Ser Thr
85 90 95

Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys Glu Cys Glu
100 105 110

Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser Phe Ile Arg
115 120 125

Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp Asp Asp Asp
130 135 140

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Tyr Ser Met Gln
145 150 155 160

Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser Ala
165 170 175

Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln
180 185 190

Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu Met
195 200 205

Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys
210 215 220

Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr
225 230 235 240

Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg
245 250 255

His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala
260 265 270

Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys Gly
275 280 285

Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr Val
290 295 300

Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser
305 310 315 320

Thr Ser Pro Gln

<210> 8

<211> 361

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/human pro IL-18)

<400> 8

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly
 145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Met Ala Ala Glu Pro Val Glu Asp
 165 170 175

Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr Leu Tyr
 180 185 190

13/40

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys
195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu
210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser
225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr
245 250 255

Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys
260 265 270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys
275 280 285

Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile
290 295 300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu
305 310 315 320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp
325 330 335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser
340 345 350

Ile Met Phe Thr Val Gln Asn Glu Asp
355 360

<210> 9

<211> 361

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/ human pro IL-18 K89A)

<400> 9

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

14/40

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Met Ala Ala Glu Pro Val Glu Asp
165 170 175

Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr Leu Tyr
180 185 190

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys
195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu
210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser
225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr
245 250 255

Ala Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys
260 265 270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys
275 280 285

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Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile
290 295 300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu
305 310 315 320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp
325 330 335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser
340 345 350

Ile Met Phe Thr Val Gln Asn Glu Asp
355 360

<210> 10

<211> 325

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/mature human IL-18)

<400> 10

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

16/40

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys
165 170 175

Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln
180 185 190

Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp
195 200 205

Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln
210 215 220

Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser
225 230 235 240

Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro
245 250 255

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg
260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr
275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu
290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr
305 310 315 320

Val Gln Asn Glu Asp
325

<210> 11

<211> 325

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/ mature human IL-18
K89A)

<400> 11

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1 5 10 15
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
 20 25 30
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
 35 40 45
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
 50 55 60
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
 65 70 75 80
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
 85 90 95
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
 100 105 110
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
 115 120 125
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
 130 135 140
 Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly
 145 150 155 160
 Gly Gly Ser Gly Gly Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys
 165 170 175
 Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln
 180 185 190
 Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp
 195 200 205
 Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Ala Asp Ser Gln
 210 215 220
 Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser
 225 230 235 240
 Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro
 245 250 255

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg
 260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr
 275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu
 290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr
 305 310 315 320

Val Gln Asn Glu Asp
 325

<210> 12

<211> 371

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine pro-IL-18)

<400> 12

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
 1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
 20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
 35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
 50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
 65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
 85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
 100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
 115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys
180 185 190

Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn
195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala
210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln
225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro
245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly
260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser
275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn
290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro
305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe
325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys
340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu
355 360 365

His Gln Ser
370

<210> 13

<211> 371

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine pro IL-18 K89A)

<400> 13

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
 1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
 20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
 35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
 50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
 65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
 85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
 100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
 115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
 130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
 145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
 165 170 175

Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys
 180 185 190

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Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn
195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala
210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln
225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro
245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly
260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser
275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn
290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro
305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe
325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys
340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu
355 360 365

His Gln Ser
370

<210> 14

<211> 336

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/ mature murine IL-18)

<400> 14

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Thr Ser Ser Ser Thr Ala
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg
180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe
195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg
210 215 220

Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val
225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn
245 250 255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp
260 265 270

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Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn
275 280 285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys
290 295 300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu
305 310 315 320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
325 330 335

<210> 15

<211> 336

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/mature murine IL-18
K89A)

<400> 15

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
 145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly
 165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg
 180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe
 195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg
 210 215 220

Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly Leu Ala Val
 225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn
 245 250 255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp
 260 265 270

Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn
 275 280 285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys
 290 295 300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu
 305 310 315 320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
 325 330 335

<210> 16

<211> 347

<212> PRT

<213> artificial sequence (fusion human IL-21/linker/ human IL-2)

<400> 16

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
 1 5 10 15

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
20 25 30

Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln
35 40 45

Gln Pro Tyr Ile Thr Asn Arg Thr Phe Met Leu Ala Lys Glu Ala Ser
50 55 60

Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe
65 70 75 80

His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu
85 90 95

Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln
100 105 110

Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg
115 120 125

Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn
130 135 140

Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu
145 150 155 160

Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn
165 170 175

Ala Cys Ile Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
180 185 190

Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu
195 200 205

Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
210 215 220

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
225 230 235 240

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
245 250 255

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
260 265 270

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
 275 280 285

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
 290 295 300

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
 305 310 315 320

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
 325 330 335

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
 340 345

<210> 17

<211> 325

<212> PRT

<213> artificial sequence (fusion murine IL-21/linker/murine IL-2)

<400> 17

Met Glu Arg Thr Leu Val Cys Leu Val Val Ile Phe Leu Gly Thr Val
 1 5 10 15

Ala His Lys Ser Ser Pro Gln Gly Pro Asp Arg Leu Leu Ile Arg Leu
 20 25 30

Arg His Leu Ile Asp Ile Val Glu Gln Leu Lys Ile Tyr Glu Asn Asp
 35 40 45

Leu Asp Pro Glu Leu Leu Ser Ala Pro Gln Asp Val Lys Gly His Cys
 50 55 60

Glu His Ala Ala Phe Ala Cys Phe Gln Lys Ala Lys Leu Lys Pro Ser
 65 70 75 80

Asn Pro Gly Asn Asn Lys Thr Phe Ile Ile Asp Leu Val Ala Gln Leu
 85 90 95

Arg Arg Arg Leu Pro Ala Arg Arg Gly Gly Lys Lys Gln Lys His Ile
 100 105 110

Ala Lys Cys Pro Ser Cys Asp Ser Tyr Glu Lys Arg Thr Pro Lys Glu

115

120

125

Phe Leu Glu Arg Leu Lys Trp Leu Leu Gln Lys Met Ile His Gln His
 130 135 140

Leu Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Tyr Ser Met
 145 150 155 160

Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser
 165 170 175

Ala Pro Thr Ser Ser Ser Thr Ser Ser Thr Ala Glu Ala Gln Gln
 180 185 190

Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu
 195 200 205

Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu
 210 215 220

Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala
 225 230 235 240

Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu
 245 250 255

Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp
 260 265 270

Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys
 275 280 285

Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr
 290 295 300

Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile
 305 310 315 320

Ser Thr Ser Pro Gln
 325

<210> 18

<211> 334

<212> PRT

<213> artificial sequence (fusion human IFN-g/linker/human IL-2)

<400> 18

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
 1 5 10 15
 Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu
 20 25 30
 Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
 35 40 45
 Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
 50 55 60
 Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
 65 70 75 80
 Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
 85 90 95
 Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
 100 105 110
 Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
 115 120 125
 Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
 130 135 140
 Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
 145 150 155 160
 Gly Arg Arg Ala Ser Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 165 170 175
 Gly Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala
 180 185 190
 Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr
 195 200 205
 Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
 210 215 220
 Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
 225 230 235 240

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Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
245 250 255

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
260 265 270

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
275 280 285

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
290 295 300

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
305 310 315 320

Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
325 330

<210> 19

<211> 334

<212> PRT

<213> artificial sequence (fusion murine IFN-g/linker/murine IL-2)

<400> 19

Met Asn Ala Thr His Cys Ile Leu Ala Leu Gln Leu Phe Leu Met Ala
1 5 10 15

Val Ser Gly Cys Tyr Cys His Gly Thr Val Ile Glu Ser Leu Glu Ser
20 25 30

Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser
35 40 45

Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys
50 55 60

Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val
65 70 75 80

Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser
85 90 95

His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala
100 105 110

Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg
 115 120 125

Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu Pro Glu
 130 135 140

Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Gly Gly Gly Gly Ser
 145 150 155 160

Gly Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr
 165 170 175

Leu Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr
 180 185 190

Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln
 195 200 205

Gln Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu
 210 215 220

Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr
 225 230 235 240

Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln
 245 250 255

Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr
 260 265 270

Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn
 275 280 285

Ile Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu
 290 295 300

Cys Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg
 305 310 315 320

Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln
 325 330

<210> 20

<211> 26

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-2)

<400> 20
cggaattcca cagtgcctc aagtcc 26

<210> 21

<211> 24

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-2)

<400> 21
ggggtacccc ttatgtgtg taag 24

<210> 22

<211> 34

<212> DNA

<213> artificial sequence (sense primer for cloning variant N88G of murine IL-2)

<400> 22
gagaatttca tcagcgtat cagagtaact gttg 34

<210> 23

<211> 34

<212> DNA

<213> artificial sequence (antisense primer for cloning variant N88G of murine IL-2)

<400> 23
caacagttac tctgataccg ctgatgaaat tctc 34

<210> 24

<211> 34

<212> DNA

<213> artificial sequence (sense primer for cloning variant N88R of murine IL-2)

<400> 24
gagaatttca tcagccgtat cagagtaact gttg 34

<210> 25

<211> 34

<212> DNA

<213> artificial sequence (antisense primer for cloning variant N88R of murine IL-2)

<400> 25

caacagttac tctgatacgg ctgatgaaat tctc

34

<210> 26

<211> 43

<212> DNA

<213> artificial sequence (sense primer for cloning variant Q126M of murine IL-2)

<400> 26

ggagatggat agccttctgt atgagcatca tctcaacaag ccc

43

<210> 27

<211> 43

<212> DNA

<213> artificial sequence (antisense primer for cloning variant Q126M of murine IL-2)

<400> 27

gggcttggtg agatgatgct catacagaag gctatccatc tcc

43

<210> 28

<211> 27

<212> DNA

<213> artificial sequence (sense primer for cloning variant D20I of murine IL-2)

<400> 28

gagcagctgt tgatgacct acaggag

27

<210> 29

<211> 27

<212> DNA

<213> artificial sequence (antisense primer for cloning variant D20I of murine IL-2)

<400> 29

ctcctgtagg atcatcaaca gctgctc

27

<210> 30

<211> 35

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-7)

<400> 30

ccgctcgagc ggatgttcca tgtttctttt agata

35

<210> 31

<211> 33

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-7)

<400> 31

cggggtaccc cgttatatac tgcccttcaa aat

33

<210> 32

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-18)

<400> 32

ccgctcgagc ggatggctgc catgtcagaa ga

32

<210> 33

<211> 43

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-18)

<400> 33
cggggtaccc cgctaacttt gatgtaagtt agtgagagtg aac 43

<210> 34

<211> 43

<212> DNA

<213> artificial sequence (sense primer for cloning variant K89A of murine IL-18)

<400> 34
ccagactgat aatatacatg tacgcagaca gtgaagtaag agg 43

<210> 35

<211> 43

<212> DNA

<213> artificial sequence (antisense primer for cloning variant K89A of murine IL-18)

<400> 35
cctcttactt cactgtctgc gtacatgtat attatcagtc tgg 43

<210> 36

<211> 50

<212> DNA

<213> artificial sequence (sense primer for cloning mature murine IL-18)

<400> 36
ggtggaggcg gttcaggcgg aggtggctct aactttggcc gacttcactg 50

<210> 37

<211> 31

<212> DNA

<213> artificial sequence (antisense primer for cloning mature murine IL-18)

<400> 37
ctaactttga tgtaagttag tgagagtga c 31

<210> 38

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-21)

<400> 38

ccgctcgagc ggatggagag gacccttgtc tg

32

<210> 39

<211> 37

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-21)

<400> 39

cggggtaccc cgctaggaga gatgctgatg aatcatc

37

<210> 40

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-15)

<400> 40

ccgctcgagc ggatgtacag catgcagctc gc

32

<210> 41

<211> 31

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-15)

<400> 41

cggggtaccc cgctacttgt catcgctcgtc c

31

<210> 42

<211> 32

<212> DNA

<213> artificial sequence (primer 5' for generating the mIL2/IL18 fusion)

<400> 42
ccgctcgagc ggatgtacag catgcagctc ga

32

<210> 43

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the lIL2/IL18 fusion)

<400> 43
ggcggaggcg gttcaggcgg aggtggctct atggctgcca tgcagaaga

50

<210> 44

<211> 50

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL2/IL18 fusion)

<400> 44
agagccacct cgcctgaac cgcctccacc ttgagggtt gttgagatga

50

<210> 45

<211> 49

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL18/IL2 fusion)

<400> 45
ggcggaggcg gttcaggcgg aggtggctct atgtacagca tgcagctcg

49

<210> 46

<211> 60

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL18/IL2 fusion)

<400> 46

agagccacct ccgcctgaac cgcctccacc actttgatgt aagttagtga gagtgaacat 60

<210> 47

<211> 31

<212> DNA

<213> artificial sequence (3' primer for generating the mIL18/IL2 fusion)

<400> 47

cggggtaccc cgttattgag ggcttggtga g 31

<210> 48

<211> 50

<212> DNA

<213> artificial sequence for generating the mIL2/mature IL18 fusion)

<400> 48

ggtggaggcg gttcaggcgg aggtggctct aactttggcc gacttcactg 50

<210> 49

<211> 31

<212> DNA

<213> artificial sequence (3' primer for generating the mIL2/ mature IL18 fusion)

<400> 49

ctaactttga tgtaagttag tgagagtga c 31

<210> 50

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IL7 fusion)

<400> 50

ggtggaggcg gttcaggcgg aggtggctct atgttccatg tttcttttag 50

<210> 51

<211> 49

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL7/IL2 fusion)

<400> 51
agagccacct ccgcctgaac cgcctccacc tatactgccc ttcaaaatt 49

<210> 52

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IL21 fusion)

<400> 52
ggtggaggcg gttcaggcgg aggtggctct atggagagga cccttgtctg 50

<210> 53

<211> 52

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL21/IL2 fusion)

<400> 53
agagccacct ccgcctgaac cgcctccacc ggagagatgc tgatgaatca tc 52

<210> 54

<211> 55

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IFN γ fusion)

<400> 54
ggtggaggcg gttcaggcgg aggtggctct atgaacgcta cacactgcat cttgg 55

<210> 55

<211> 33

<212> DNA

<213> artificial sequence for generating the mIL2/IFN γ fusion)

<400> 55
cggggtaccc cgtcagcagc gactcctttt ccg 33

<210> 56

<211> 37

<212> DNA

<213> artificial sequence (5' primer for cloning the mIFNg/IL2 fusion)

<400> 56
ccgctcgagc ggatgaacgc tacacactgc atcttgg 37

<210> 57

<211> 49

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIFNg/IL2 fusion)

<400> 57
agagccacct ccgcctgaac cgctccacc gcagcgactc cttttcgc 49

<210> 58

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IL15 fusion)

<400> 58
ggtggaggcg gttcaggcgg aggtggctct atgtacagca tgcagctcgc 50

<210> 59

<211> 49

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL15/IL2 fusion)

<400> 59

agagccacct ccgcctgaac cgcctccacc cttgtcatcg tcgtccttg